Brooke-Spiegler syndrome

Brooke-Spiegler syndrome is a condition involving multiple skin tumors that develop from structures associated with the skin (skin appendages), such as sweat glands and hair follicles. People with Brooke-Spiegler syndrome may develop several types of tumors, including growths called spiradenomas, trichoepitheliomas, and cylindromas. Spiradenomas develop in sweat glands. Trichoepitheliomas arise from hair follicles. The origin of cylindromas has been unclear; while previously thought to derive from sweat glands, they are now generally believed to begin in hair follicles. The tumors associated with Brooke-Spiegler syndrome are generally noncancerous (benign), but occasionally they may become cancerous (malignant). Affected individuals are also at increased risk of developing tumors in tissues other than skin appendages, particularly benign or malignant tumors of the salivary glands.

People with Brooke-Spiegler syndrome typically begin developing tumors in early adulthood. The tumors are most often found on the head and neck. They grow larger and increase in number over time. In severe cases, the tumors may get in the way of the eyes, ears, nose, or mouth and affect vision, hearing, or other functions. The tumors can be disfiguring and may contribute to depression or other psychological problems. For reasons that are unclear, females with Brooke-Spiegler syndrome are often more severely affected than males.

Frequency

Brooke-Spiegler syndrome is a rare disorder; its prevalence is unknown.

Genetic Changes

Brooke-Spiegler syndrome is caused by mutations in the *CYLD* gene. This gene provides instructions for making a protein that helps regulate nuclear factor-kappa-B. Nuclear factor-kappa-B is a group of related proteins that help protect cells from self-destruction (apoptosis) in response to certain signals. In regulating the action of nuclear factor-kappa-B, the CYLD protein allows cells to respond properly to signals to self-destruct when appropriate, such as when the cells become abnormal. By this mechanism, the CYLD protein acts as a tumor suppressor, which means that it helps prevent cells from growing and dividing too fast or in an uncontrolled way.

People with Brooke-Spiegler syndrome are born with a mutation in one of the two copies of the *CYLD* gene in each cell. This mutation prevents the cell from making functional CYLD protein from the altered copy of the gene. However, enough protein is usually produced from the other, normal copy of the gene to regulate cell growth effectively. For tumors to develop, a second mutation or deletion of genetic material

involving the other copy of the *CYLD* gene must occur in certain cells during a person's lifetime.

When both copies of the *CYLD* gene are mutated in a particular cell, that cell cannot produce any functional CYLD protein. The loss of this protein allows the cell to grow and divide in an uncontrolled way to form a tumor. In people with Brooke-Spiegler syndrome, a second *CYLD* mutation typically occurs in multiple cells over an affected person's lifetime. The loss of CYLD protein in different types of cells in the skin leads to the growth of a variety of skin appendage tumors.

Some researchers consider Brooke-Spiegler syndrome and two related conditions called multiple familial trichoepithelioma and familial cylindromatosis, which are also caused by *CYLD* gene mutations, to be different forms of the same disorder. It is unclear why mutations in the *CYLD* gene cause different patterns of skin appendage tumors in each of these conditions, or why the tumors are generally confined to the skin in these disorders.

Inheritance Pattern

Susceptibility to Brooke-Spiegler syndrome has an autosomal dominant pattern of inheritance, which means one copy of the altered gene in each cell increases the risk of developing this condition. However, a second, non-inherited mutation is required for development of skin appendage tumors in this disorder.

Other Names for This Condition

- BRSS
- BSS
- Spiegler-Brooke syndrome

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Spiegler-Brooke syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1857941/

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html

- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Benign Tumors
  https://medlineplus.gov/benigntumors.html
- Health Topic: Skin Conditions
  https://medlineplus.gov/skinconditions.html

Genetic and Rare Diseases Information Center

- Brooke-Spiegler syndrome
  https://rarediseases.info.nih.gov/diseases/10179/brooke-spiegler-syndrome

Educational Resources

- American Cancer Society: Skin Cancer
  https://www.cancer.org/cancer/basal-and-squamous-cell-skin-cancer.html
- Disease InfoSearch: Spiegler-Brooke syndrome
  http://www.diseaseinfosearch.org/Spiegler-Brooke+syndrome/6719
- MalaCards: brooke-spiegler syndrome
  http://www.malacards.org/card/brooke_spiegler_syndrome

Patient Support and Advocacy Resources

- AboutFace
  http://www.aboutface.ca/
- Skin Cancer Foundation
  http://www.skincancer.org/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Skin+Neoplasms%5BMAJR%5D%29+AND+%28%28brooke-spiegler+syndrome%5BTIAB%5D%29+OR+%28brss%5BTIAB%5D%29+OR+%28bss%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- BROOKE-SPIEGLER SYNDROME
  http://omim.org/entry/605041

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Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/brooke-spiegler-syndrome

Reviewed: June 2012
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
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National Institutes of Health
Department of Health & Human Services